Does packaging with a calendar feature improve adherence to self-administered medication for long-term use? A systematic review

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CRD summary
The review concluded that calendar packaging, especially in combination with education and other reminder strategies, may improve medication adherence; methodological limitations precluded conclusions about effect sizes and clinical benefits or harms. The authors acknowledged the limitations in the evidence base and their conclusions were suitably cautious.

Authors' objectives
To assess the evidence of the adherence benefits and harms of calendar blister packaging and calendar pill organisers for self-administered long-term medication use.

Searching
MEDLINE, Web of Science, The Cochrane Library and Current Controlled Trials were searched to September 2010 for articles published in English. Search terms were reported. Reference lists of sentinel trials and retrieved reviews were searched. Researchers in the field were contacted to identify further studies.

Study selection
Randomised controlled trials (RCTs) of solid, self-administered, oral medication packaged with calendar blister packaging or calendar pill organisers versus control in community dwelling adult patients (over 18 years) who took daily medication for any duration longer than one month were eligible for inclusion. Calendar pill organisers had to incorporate a reminder system for day of week as part of packaging. Trials had to report at least one objective quantitative outcome measure of medication adherence.

The included trials studied calendar blister packaging and calendar pill organisers versus standard vial of loose pills in patients treated with medication for hypertension, type 2 diabetes, epilepsy, serious mental illness and vitamin prophylaxis. The concomitant interventions given alongside calendar blister packaging or calendar pill organisers included education, mailed refill reminders, phone calls if missed refill and customised dosing schedule. Publication dates of trials ranged from 1980 to 2009.

Two reviewers independently performed study selection. Disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
Trial quality was assessed using Jadad criteria of randomisation, allocation concealment, adherence outcomes, description of withdrawals/drop-outs and intention-to-treat to give a maximum score of 5.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on adherence outcomes, clinical outcomes and harms. Study authors were contacted for further information, where required.

Two reviewers independently performed data extraction. Disagreements were resolved by discussion.

Methods of synthesis
A narrative synthesis was presented with trials grouped by outcomes. Meta-analysis was not performed due to heterogeneity in patient populations.

Results of the review
Ten RCTs (492 patients) were included in the review. The quality of the included trials was very poor to moderate: two trials scored zero, two scored 1, two scored 2 and four scored 3 out of 5. Trial sample size ranged from 13 to 89 patients. Trial duration ranged from two to 12 months.

Compared with control, six out of eight evaluable trials had positive adherence outcomes and one out of nine evaluable trials had positive clinical outcomes. None of the trials provided suitable data to evaluate harms.

Authors' conclusions
Calendar packaging, especially in combination with education and other reminder strategies, may improve medication adherence, but methodological limitations precluded conclusions about effect sizes and clinical benefits or harms.

CRD commentary
Inclusion criteria for the review were clearly defined and several relevant data sources were searched. There was a risk of language bias, as only articles in English were included. Publication bias was not assessed and could not be ruled out. Attempts were made to reduce reviewer error and bias throughout the study selection and during data extraction; the authors did not report whether or not the same methods were used for quality assessment.

Quality assessment was undertaken using a standard checklist, which indicated the generally poor quality of the included trials (acknowledged by the authors). Trials were synthesised narratively due to the marked heterogeneity across them, which seemed reasonable.

The authors acknowledged the limitations in the evidence base and their conclusions were suitably cautious. One author declared funding from Astra Zeneca, Roche and Pfizer.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.
Research: The authors stated that high methodological quality trials of adequate size and duration (at least six months) were needed. A standardised adherence outcome measure was needed. Medication-adherence packaging should be combined with other adherence interventions, such as education and behaviour. Components of the most effective adherence strategies can be assessed in factorial studies. Morbidity endpoints and health economics should be assessed. The effects of different dosing schedules and numbers of calendar packaged daily medications needed exploration.

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